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USSR WORK ON DRUG THERAPY OF INJURIES OF THE NERVOUS SYSTEM

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By using some drugs (particularly eserine and proserine) one may achieve restoration of functions of the nervous system which have been impaired as the result of trauma or of an organic disease. The effect of the drugs in question is observed even at stages of the disease during which an exclusive action of the therapeutic agent on inflammatory processes or other local processes at the site of the injury cannot be expected. Thus, a pronounced restoration of functions in the residual period of poliomyelitis has been obtained many years after the infection. Later, analogous results were obtained at clinics by using the original Soviet drug dibasol. The restorative effect of dibasol on the nervous system was discovered by M. A. Rozin and K. V. Tsomaya.

Workers at Yu. M. Uflyand's laboratory found that as a result of treatment with dibasol the electrical component of the knee reflex, which was totally absent 9 years after infection with poliomyelitis, could be made to reappear. In one case there was considerable improvement subsequent to this type of treatment even 17 years after the infection. The explanation of the effectiveness of the treatment is that foci of prolonged inactivity of nerve elements in the lower ranges of the nervous system can still be restored to activity by applying certain substances. Attempts to clarify the mechanism of the action of these substances have been made by M. A. Rozin and other workers in this field.

We first tried to establish whether a definite effect on chemical processes is not the common factor of all types of restorative therapy that are effective in injuries of the nervous system. Unfortunately, the exact nature of the chemical processes in question is not yet known. We know definitely that the action of acetylcholine, the processes of its formation, and its enzymatic inactivation play an important role in the transmission of nerve impulses at the majority of synapses. Under the circumstances, we may very well assume that all agents which restore nerve activity are cholinesterase inhibitors.

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Inhibition of cholinesterase would lead to an accumulation of acetylcholine in nerve cells, and the large doses of acetylcholine would in turn bring the nerve cells out of their state of protracted inactivity.

Investigation carried out by M. A. Rozin and S. M. Vishnyakov on animals with an experimental injury of the sciatic nerve showed that eserine and proserine have a strong anticholinesterase activity. On the other hand, the anticholinesterase activity of dibasol is negligible. The conclusion that dibasol exerts no anticholinesterase effect follows from clinical observations. As distinguished from eserine and proserine, dibasol produces no side effects, such as salivation, perspiration, reddening of the face, bradycardia, etc., which are typical of the "muscarine" action due to stabilized acetylcholine. Nevertheless, dibasol is much more active than eserine or proserine in restoring motion that has been impaired by the injury of a peripheral motor neuron.

Another way of explaining the mechanism of the action of the drugs in question would be by assuming that the inactive sections of the nervous system are foci of pathological inhibition, of the type referred to as "inert" by I. P. Pavlov. Experiments by Ye. Ye. Belen'kiy showed that immersion in a 1 : 10,000,000 dibasol solution of a nerve section in a state of parabiosis resulted in restoration of the nerve section's conductivity. This conductivity usually disappears when the nerve is dipped into a physiological salt solution. Application of dibasol prevented development of Sechenov's inhibition in frogs after the inhibition had been induced in the customary manner by placing a crystal of sodium chloride on the section through the optical bulges. S. M. Vishnyakov showed that there is no correlation between the capacity of some substances to prevent Sechenov's inhibition and their anticholinesterase activity. In M. A. Rozin's experiments dibasol, on being applied 3 days after a strong electric current had been passed through on of the legs of a frog, brought about weakening of the resulting reflectory paresis, which had also affected the corresponding (uninjured) leg on the other side.

S. M. Vishnyakov also studied the effect of dibasol on the central inhibition produced in rabbits by a strong pain irritation (application of an electric current). The inhibition resulted in a pronounced and protracted weakening of the summation /addition/ of impulses when a bending reflex was induced in a hind extremity by means of a sub-threshold irritation. The inhibition could be eliminated by the application of dibasol; under the action of this drug, the number of impulses required to produce a reflex reaction was lowered approximately to the initial level which existed before the inhibition was established. The action of dibasol was plainly noticeable even 3 days after a single intravenous injection of this drug had been carried out. The results of these experiments show clearly that the action of dibasol is based on its capacity to eliminate the inert pathological inhibition which remains in some sections of the nervous system for a long time after this system has been injured.

Dibasol and similar substances may prove to be useful "chemical analysts" in physiological investigations; they were found to be of help in the search for new drugs. A. Ye. Uglov and S. M. Vishnyakov, in testing the effects of a new group of chemical compounds on various types of inhibition, found that these compounds exert a therapeutic effect in experimentally induced injuries of peripheral motor neurons.

Naturally, a drug which will remove with equal facility all types and manifestations of the inhibitory process in the organism can be of only toxicological interest; any drug which is to be of value from the practical standpoint must exhibit a selective action. In view of the fact that the degree and type of selectivity vary with chemical composition, further research on the subject will enrich USSR medicine with an extensive array of drugs having a wide range of differentiated activity which will make them suitable for the treatment of a great number of diseases of the nervous system.

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